BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

7953.0004.9999

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

09/500,936

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER

ART UNIT | PAPER NUMBER

ALBERT P. HALLUIN
HOWREY & SIMON
1299 PENNSYLVANIA AV. NW
WASHINGTON DC 20004-2402

RECEIVED
DOCKET DEPT.
JUL - 2 1999
HOWREY & Simon

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

RECEIVED
JUL 0 6 1999
HOWREY & SIMON (M.P.)

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 11/12/98

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-27 is/are pending in the application.
Of the above, claim(s) 10-20 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-9, 21-27 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

ted For 9/28/99 (NO)
Last date 12/28/99

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3 4 8 9 10
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

DOCKETED gdc 7.2.99
Response Due 9.28.99
Last Day 12.28.99

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

The Office Action of January 22, 1999 is hereby vacated to permit consideration of the Preliminary Amendment filed November 12, 1998.

The Group and/or Art Unit location of your application in the Patent and Trademark Office has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1641.

The Examiner acknowledges receipt of the following submissions: The response to the Restriction filed November 3, 1998; the Preliminary Amendment filed November 12,1998; the Information Disclosure Statements filed October 5, 1998, November 16, 1998 and April 19, 1999; and the Change of Address filed February 9, 1999.

Election/Restriction

Applicant's election without traverse of Group I (claims 1-9, and 16) in Paper No. 7 is acknowledged.

Newly amended claim 16 is directed to an invention that is independent or distinct from the invention originally claimed.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 16 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

This application contains claims 10-20 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

In this application:

Claims 7-9 and 16 were amended.

Claims 10-15, and 16-20 are withdrawn from consideration by the Examiner.

Claims 21-27 were added.

Claims 1-9 and 21-27 are under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The oath/declaration was not signed by the coinventor David A. Benaron.

Drawings

The drawings are objected to under 37 CFR 1.84 or 1.152 for the reasons stated on PTO 948. Correction is required.

Specification

A substitute specification including claims is required pursuant to 37 CFR 1.125(a) because:

In the Preliminary Amendment of November 12, 1998, Applicant indicates the inadvertent misnumbering of the lines of the specification. Specifically, Applicant indicates that each page contains approximately five lines fewer than what is implied by the numbers in the left margin. Applicant proposes to remedy the misnumbering by henceforth referring to the actual lines of text instead of the line numbers in the margin. This proposal,

however, may result in confusion if Applicant files any amendment to the specification. Therefore, in order to prevent any confusion or misunderstandings, a substitute specification is required.

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Claim Rejections - 35 USC § 112

Claims 1-9 and 21-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for the deposit of the biodetector. Because it is not clear that the biodetector possessing the properties of the claimed invention are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the best mode disclosed by the specification requires the use of the biodetector, a suitable deposit for patent purposes is required. Accordingly, filing of evidence of the reproducible production of the biodetector, one of ordinary skill in the art could be assured to the ability to practice the invention as claimed.

If the deposit has been made under the provisions of the Budapest Treaty, an affidavit or declaration filed by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, and that all restrictions will be irrevocably removed upon the granting of a patent on this application is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the

deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) The deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longer; and

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biodetector described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claims 21, 22, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s),

(d) The deposits will be replaced if they should become non-viable or non-replicable.

In addition, a deposit of the biological material that is capable of self-replication either directly or indirectly must be viable at the time of the deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;

2) The name and address of the depositor;

3) The date of deposit;

4) The identity of the deposit and the accession number given by the depository;

5) The date of the viability test;

6) The procedures used to obtain a sample if the test is not done by the depository; and

7) A statement that the deposit is capable of reproduction.

at the time the application was filed, had possession of the claimed invention.

Claims 21 recites the limitation "said membrane signal transducer is derived from PhoQ". However, the specification as originally filed does not provide support for this limitation.

Claim 22 recites the limitation "sheltered in a genetically engineered bacterial cell". However, the specification as originally filed does not provide support for this limitation.

Claim 25 recites the limitation "said enzymatic signal transforming domain comprises an active domain of PhoQ". However, the specification as originally filed does not provide support for this limitation.

Claim 26 recites the limitation "said fusion protein is a fusion of an active domain of PhoQ, and a region of a heavy chain antibody". However, the specification as originally filed does not provide support for this limitation.

Claims 1-9, and 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the" detection of a selected substance. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 22-24 and 27 are rejected under 35 U.S.C. 103 as being obvious by Karube et al and Sleight et al.

Karube et al (Current Opinion in Biotechnology 5(1):54-59, 1994) teach biosensor cells used for the detection and analysis of specific substrates. The biosensors are comprised of a microorganism sensing element which recognize specific substrates, and a transducer to convert the biochemical signal produced into an electronic signal. (See especially page 54, first column)

Karube et al teach that the transducer can be a photodetector, potentiometric electrodes, amperometric electrodes and thermistors. (See especially page 54, second column)

The reference also discloses that the visible reaction observed can be luminescence by fusing the luxAB gene to the flxAB gene. (See especially page 56, first column)

Karube et al disclose biosensors, however, the reference differs in not teaching an extracellular ligand-specific moiety and an intracellular signal transforming domain.

Sleight et al (Sleight et al. Signal Transduction. In: Cell Physiology Source Book. N. Sperelankis (ed). 1995.) teach that a variety of substances act as extracellular signals by binding to specific receptors located on the cell surface. By a process known as signal transduction, the extracellular signal stimulates an intracellular change which leads to the formation or release of an intracellular signal. (See especially page 117)

Given the teachings of the prior art that cells convert extracellular signals to intracellular physiological responses and biosensors are comprised of immobilized cells, it would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a biosensor comprised of an extracellular ligand-specific moiety, and an intracellular signal transforming domain as the art teaches that bacterial cells use a process known as signal transduction to convert an external chemical signal created by the binding of a specific substrate to an intracellular signal to effect the function of a large number of proteins and the use of luceriferase produces a light response which can easily be detected.

Claims 21 and 25 are rejected under 35 U.S.C. 103 as being unpatentable by Karube et al and Sleight et al (as applied to claims 1-9) and further in view of Miller et al.

The teachings of Karube et al and Sleight et al were set forth above. The references, however, differ in not teaching the PhoQ 2-component regulatory system.

Miller et al (Proc. Natl. Acad. Sci 86:5054-58, 1989) teach a two-component regulatory system comprised of PhoP and PhoQ. PhoQ functions as a membrane-associated protein kinase that phosphorylates PhoP in response to environmental signals. The PhoP then activates promoters. The reference also suggests that the periplasmic domain of PhoQ may be involved in sensing environmental parameters. (See especially page 5058)

Given the teachings of the prior art that PhoQ functions in response to environmental parameters, it would have been obvious to one of ordinary skill in the art at the time the invention was made to create a biosensor comprised of the PhoQ as the signal transducer as the art recognized the function of the PhoP/PhoQ in regulating genes involved in virulence and the function of the PhoQ in phosphorylating PhoP in response to environmental signals.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to V. Ryan whose telephone number is (703)305-6558.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-0196.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Papers related to this application may be submitted to the Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax number for Art Unit 1641 is (703)308-4242.

V. Ryan
Patent Examiner/Art Unit 1641
June 1999
Ryan/vr